Double C–H Activation

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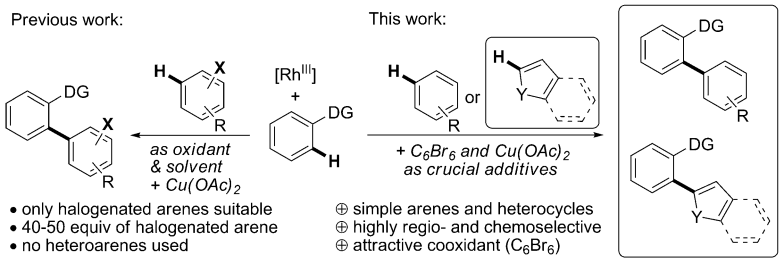
Rhodium(III) and Hexabromobenzene—A Catalyst System for the Cross-Dehydrogenative Coupling of Simple Arenes and Heterocycles with Arenes Bearing Directing Groups**

*Joanna Wencel-Delord, Corinna Nimphius, Honggen Wang, and Frank Glorius**

The biaryl scaffold is of great importance in many fields, such as biologically active molecules and materials. Lately, its synthesis has been greatly facilitated by the advent of cross-coupling reactions. Nevertheless, the development of more step-and atom-economic transformations is highly desirable. The development of direct arylation reactions (coupling of a preactivated partner with a benzene derivative) was a first approach to this goal.[1] However, more recently, catalyst systems that enable the oxidative cross-dehydrogenative coupling (CDC) of two non-prefunctionalized arenes have emerged as an attractive alternative.[2] Initial studies in this challenging field showed that palladium catalysts are particularly suited for this transformation.[3,4] Furthermore, very recently, [$Rh^{III}Cp^*$]-catalyzed ($Cp^* = C_5Me_5$) formations of biaryls through twofold C–H activation were developed.[5–8] The key to success was the application of aryl halides as the C–H coupling partner.[9] Indeed, these halogenated substrates are believed to not only act as the coupling partner, but also as the cooxidant and/or catalyst modifier (Scheme 1).[10] This intriguing and multiple role of the haloarenes was, however, a limitation of the catalyst system, since only halogen-substituted benzene derivatives could be used successfully. Herein, we report an unprecedented application of hexabromobenzene (C_6Br_6) as the key additive that enables a highly chemo- and regioselective dehydrogenative cross-coupling of benzamides with a variety of simple benzene derivatives. Furthermore, this unique and crucial reactant opens the door for the application of this modern strategy to the direct functionalization of synthetically useful heterocycles. Besides tremendously expanding the scope of this CDC, the use of this halogenated species allows the amount of the coupling partner to be decreased (in some cases down to 3 equiv).

In regard to the rapidly growing interest in CDC reactions, on the one hand, and their potential, highly promising industrial applications, on the other, the development of general CDCs involving an undirected C–H activation of simple arenes is an important goal. Thus, inspired by our previous studies, we commenced with an evaluation of different haloarenes and hypervalent iodine species as additives/oxidants in the Rh^{III}-catalyzed cross-coupling of benzamide **1a** with toluene.[11] An extensive optimization study enabled polybrominated benzene derivatives to be identified as the optimal, hardly toxic, and inexpensive



Scheme 1. DG = directing group. The newly formed bonds and the H atoms involved in the coupling are shown in bold.

additives/cooxidants (used together with $Cu(OAc)_2$) required for the efficient formation of the desired biaryl scaffold.[12] Notably, the addition of only two equivalents of C_6Br_6 was sufficient to achieve full conversion of **1a** into the desired biaryl moiety. Furthermore, the application of an additional aromatic solvent such as 2-chloro-*p*-xylene turned out to be beneficial, thus enabling the use of a smaller excess of the simple arene coupling partner. In addition, the use of a cosolvent also ensured a more robust reaction system and opened up the possibility of using solid, high melting arenes as coupling partners. Under the optimized conditions, the cross-coupling reaction of benzamide **1a** with benzene led to the formation of biaryl **3a** in 70% yield. The control reactions carried out in the absence of either a rhodium source or $Cu(OAc)_2$ showed the catalyst system to be total inactive. Moreover, only trace amounts of products could be detected

[*] Dr. J. Wencel-Delord,[+] C. Nimphius,[+] Dr. H. Wang, Prof. Dr. F. Glorius
Universität Münster, Organisch-Chemisches Institut
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: glorius@uni-muenster.de
Homepage: http://www.uni-muenster.de/Chemie.oc/glorius/index.html

[+] These authors contributed equally to this work.

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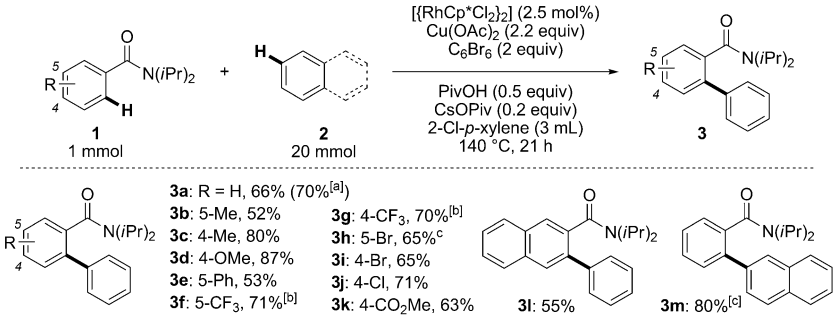
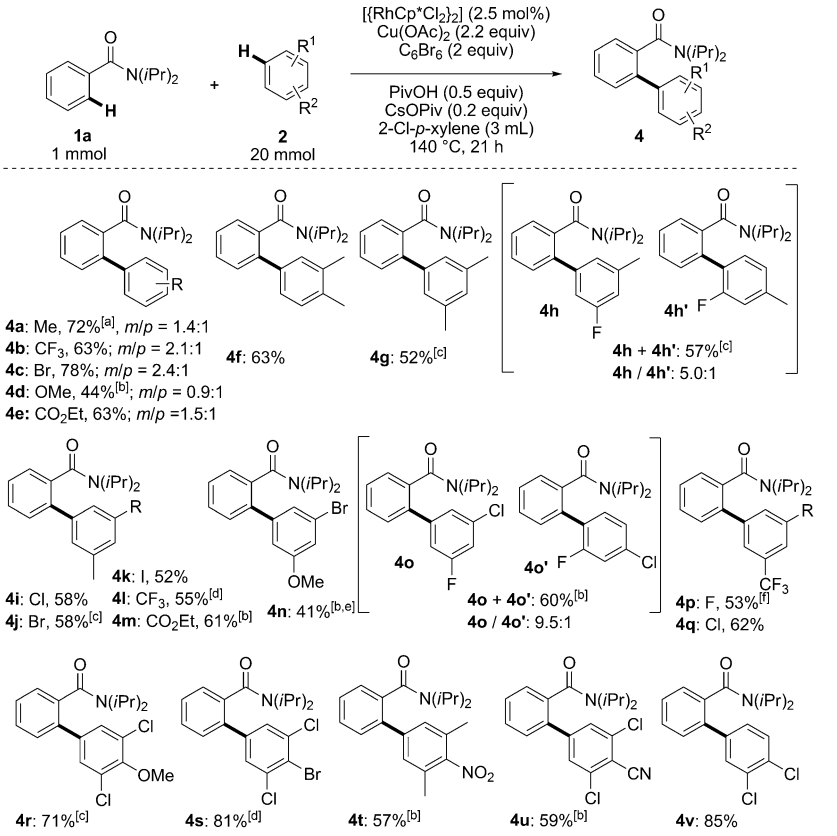
when the C_6Br_6 additive was omitted from the reaction mixture. In contrast, the absence of the silver salt led to the formation of the expected product in only a slightly lower yield (66% yield). As a consequence of the high price of silver, further studies were conducted under silver-free conditions. Finally, it was found that the presence of both pivalic acid (PivOH) and cesium pivalate (CsOPiv) is not essential, but they do, however, improve the efficiency of the overall transformation (**3a** was isolated in 58 and 62% yield in the absence of pivalic acid and cesium pivalate, respectively).

Under these optimized conditions, the cross-coupling of an array of synthetically valuable benzamides with benzene was examined (Scheme 2, **3a**–**k**). A large range of substituents at either the *meta* or *para* position of the aromatic ring was well tolerated. Electron-donating groups such as Me or OMe in the *para* position led to the formation of the desired coupling product in good yields. Importantly, the phenyl substituent was also well tolerated on the aromatic ring of the benzamide, with the additional sp^2 carbon atoms not perturbing the selectivity of the overall transformation—the expected biaryl **3e** was obtained as a single regioisomer. The arylation of the benzamides bearing strongly electron-withdrawing CF_3 groups was slightly more sluggish, and an increased reaction temperature (160°C) was required to achieve full conversion. Importantly, when brominated or chlorinated benzamides were submitted to the standard reaction conditions, the expected biaryl compounds **3h**–**j** could be isolated in synthetically useful yields, and no dehalogenated products were detected. The application of the benzamide bearing a second potential directing group such as an ester substituent led to the selective coupling reaction in the *ortho* position with respect to the amide moiety (**3k**). Extending the substrate range from the phenyl to the naphthyl system was also tolerated, and the naphthyl-benzene biaryl **3l** could be generated selectively as one isomer in 55% yield. When the benzene coupling partner was replaced by a naphthyl moiety, the desired product **3m** was formed in good selectivity (isolated product contains 7% of another isomer).



Scheme 2. Reaction of benzamides with benzene and naphthalene. General reaction conditions: benzamide **1** (1.0 mmol, 1.0 equiv), **2** (20.0 mmol, 20 equiv), [{RhCp*Cl_2}$_2$] (0.025 mol, 0.025 equiv), $Cu(OAc)_2$ (2.2 mmol, 2.2 equiv), C_6Br_6 (2.0 mmol, 2.0 equiv), PivOH (0.5 mmol, 0.5 equiv), CsOPiv (0.2 mmol, 0.2 equiv), 2-Cl-*p*-xylene (3 mL) 140°C, 21 h; isolated yields; [a] 2 mL (22 mmol) of benzene and 0.1 mmol of $AgSbF_6$ were used; [b] at 160°C; [c] product isolated together with 7% of another isomer (ratio determined by ^{1}H NMR).

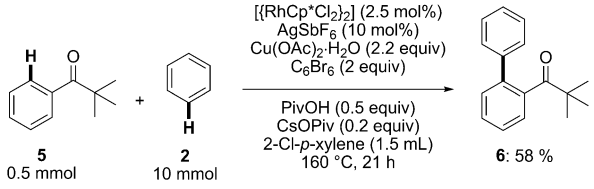


Scheme 3. CDC of benzamide **1a** with a range of benzene derivatives. General reaction conditions: see Scheme 2; isolated yields; [a] 0.5 mmol scale, 1 mL of toluene was used; [b] at 160°C; [c] at 150°C; [d] reaction carried out on a 0.5 mmol scale; [e] product isolated together with 10% of another isomer (ratio determined by ^{1}H NMR); [f] product isolated together with 7% of another isomer (ratio determined by ^{1}H NMR).

Encouraged by the good tolerance of our catalyst system towards different functional groups, the scope of simple benzene derivatives as coupling partners was evaluated (Scheme 3). Unsurprisingly, the standard benzamide **1a** underwent the CDC smoothly in the presence of monosubstituted benzene derivatives and led to the formation of the expected biaryl products (**4a**–**4e**) in satisfying yields but, independent of the nature of substituents, as mixtures of *meta*

and *para* products. However, the application of *o*- and *m*-xylene as the coupling partner enabled the regioselective formation of biaryl products **4f** and **4g**, respectively.[13] In contrast, when 3-fluorotoluene was used as the coupling partner, the formation of a second, minor isomer could be detected (**4h** and **4h′** were isolated in a 5.0:1 ratio), probably arising from the lower steric hindrance of the *ortho* position because of the fluoro substituent. The complete selectivity was reinstalled when 3-bromo- and 3-chlorotoluene were used. Importantly, even the iodo substituent was tolerated on the arene coupling partner.[14] Unlike the majority of palladium-catalyzed CDC transformations, the application of the less electron-rich toluene derivatives was also possible: the coupling of 3-(trifluoromethyl)toluene was efficient at a reaction temperature of 140 °C. Notably, the toluene derivative bearing an ester group underwent a nonchelate-assisted C–H activation that led to the *meta*-selective coupling reaction with **1**. Intriguingly, the coupling reaction of benzamide **1** with 3-bromoanisole was sluggish, and the expected product **4n** was formed in moderate yield. However, good reactivity could be reinstalled by introducing two chloro substituents in the 2- and 6-positions of anisole (**4r** was isolated in 71%). This observation would suggest that the coordination ability of the OMe group is, at least partially, responsible for the lower activity of anisole derivatives. Similarly, 2,6-substituted nitrobenzene and cyanobenzene derivatives smoothly underwent the arylation reaction.

To our delight, the efficiency of this catalytic system was also conserved when the amide directing group was replaced by a ketone. Indeed, the carbonyl substrate **5** underwent the

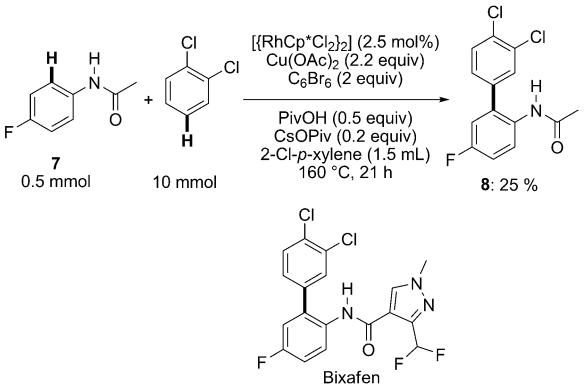


Scheme 4. CDC of ketone **5** with benzene.

monoarylation reaction smoothly to give the expected, biphenyl ketone **6** in a synthetically useful yield (Scheme 4).

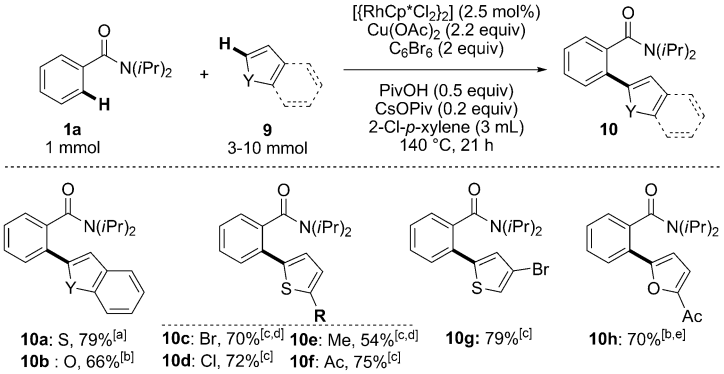
The undeniable potential of this strategy could be further illustrated by its application in the synthesis of biaryl **8**—the key intermediate of the fungizid molecule Bixafen. Under non-optimized conditions, this highly valuable product could be prepared in one step from commercially available and inexpensive 4-fluoroacetanilide **7** and 1,2-dichlorobenzene (Scheme 5). Even though the efficiency of this transformation is still limited, it shows clearly the potential of this reaction for the atom- and step-economic industrial applications of the twofold C–H activation.

We then turned our attention to using heterocycles as the coupling partners for this CDC reaction. Indeed, the presence of heterocycles in pharmaceutical, biologically active compounds and materials



Scheme 5. Application of the Rh^{III}-catalyzed direct arylation for the synthesis of **8**, key intermediate of Bixafen. 7% of the diarylated product was isolated.

makes the direct transformations of this class of compounds of prime importance. Despite considerable effort in this field over the past few years, these reactions remain rare. In particular, highly efficient and selective methods for the direct arylation of heterocycles are still an enormous challenge.[2e] Up to now, palladium has been the most generally used metal for the direct C–H activation of heterocycles, while the potential of Rh^{III} catalysts for this transformation was highlighted only recently.[15] To our delight, the coupling between **1** and benzothiophene turned out to be highly efficient and selective even if only five equivalents of the heterocycle were used. The corresponding product **10a** could be isolated in 79% yield as a single isomer (Scheme 6). The crucial role of the C_6Br_6 additive was also confirmed for this transformation: only traces of the desired product could be detected in the absence of this cooxidant. Benzofuran also turned out to be a suitable coupling partner; however, a larger amount (10 equiv) was required for the isolation of **10b** in a satisfying yield of 66%. Furthermore, this catalyst system could be applied to selectively and efficiently install an aromatic ring at the 2-position of a series of 2- and 3-substituted thiophenes, challenging substrates for CDC. In



Scheme 6. CDC of benzamide **1a** with heterocycles. General reaction conditions: see Scheme 2; yield of isolated product; [a] 5 mmol of heteroarene were used; [b] 10 mmol of heteroarene were used; [c] 3 mmol of heteroarene were used; [d] product isolated together with 5–7% of another isomer (ratio determined by ^1H NMR); [e] 30 h reaction time.

this case, a further decrease in the amount of the heterocyclic coupling partner was possible (down to 3 equiv). Notably, bromo and chloro substituents on the thiophene ring were well tolerated, and led to the formation of **10c**, **10d**, and **10g**—highly valuable building blocks for further functionalization. Finally, an electron-deficient furan was also efficiently coupled with **1** (**10h**).

To gain some mechanistic insight, a series of deuteration experiments was conducted. Significant kinetic isotope effects (KIEs) were measured for both coupling partners, thus indicating that the reaction proceeds by a true twofold C–H activation mechanism.[16,17] Furthermore, a comparison of the initial rates of the reactions (using standard and deuterated coupling partners) suggests the involvement of the nonchelate-assisted C–H activation in the rate-determining step.[17]

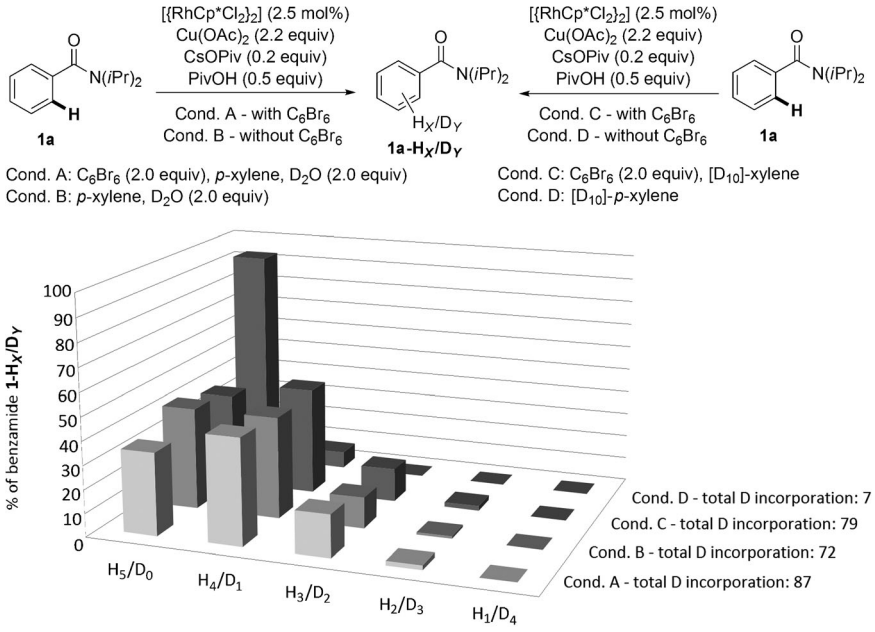


Figure 1. Impact of C_6Br_6 on the rate of C–H bond activation.

Additionally, a few competition experiments were carried out to gain more information about the influence of the electronic properties of each coupling partner on the overall reaction.[17] Firstly, treatment of 1:1 mixtures of differently substituted benzamides with benzene clearly showed that this CDC is enhanced for electron-rich benzamides. In contrast, the electronic influence on the nondirected C–H activation step is much less pronounced. When *m*-xylene and the electron-poor 3-(trifluoromethyl)toluene were submitted to the reaction conditions concomitantly (as substrate **2**), both expected products were formed in almost equal amounts. This result suggests that neither an Ar–H deprotonation pathway nor a S_EAr mechanism is plausible for this step. The observation of a significant KIE for this coupling partner led to the postulation of a σ-bond metathesis-type mechanism.[18] Further competition experiments using 3-bromotoluene as another competing partner resulted in a twofold increase in the reaction rate for this halogenated arene. While the reason for this difference is still unclear, the influence of the weak nonbonding C–Br···π interactions between this haloarene and the catalyst and/or benzamide cannot be excluded.[19]

Furthermore, it should be mentioned that product formation was always associated with the formation of C_6HBr_5 derived from the protodehalogenation of C_6Br_6, which indicates the role of C_6Br_6 as an oxidant. Additional mechanistic investigations were performed to further elucidate the roles of C_6Br_6 and $Cu(OAc)_2$.[17] Firstly, a series of stoichiometric reactions (utilizing only 5 mol% of **1a**) showed that omission of either C_6Br_6 or $Cu(OAc)_2$ led to a significant decrease in the reaction efficiency (yield of 36 and 21%, respectively, compared to 78% yield for the stoichiometric reaction under otherwise identical reaction conditions) and no reaction was observed in the absence of both the Cu salt and C_6Br_6. These observations suggest that the role of both reagents is not limited to the reoxidation of the rhodium catalyst after the reductive elimination of the product. Furthermore, the activity of the catalyst system was totally shut down by the replacement of $Cu(OAc)_2$ by $CuBr_2$, thus indicating that $CuBr_2$ is not the active species.

Finally, the impact of the presence of C_6Br_6 on the C–H activation was investigated (Figure 1). A series of reactions using D_2O as the D source in the absence of any substrate **2** showed that H/D scrambling on the benzamide was slightly enhanced in the presence of C_6Br_6 (Figure 1, conditions A versus conditions B). Interestingly, when using $[D_{10}]$-*p*-xylene[13] as a coupling partner and the only D source, we observed D transfer from $[D_{10}]$-*p*-xylene to **1**, which indicates that the C–H activation of $[D_{10}]$-*p*-xylene occurred but no reductive elimination took place. However, the rate of the undirected C–H bond activation was significantly decreased when this polybrominated reagent was omitted (Figure 1, conditions C versus conditions D). These observations could be interpreted as indirect proof of the key role of C_6Br_6 in the "activation" of the rhodium catalyst for the undirected C–H activation.

In conclusion, a new Rh^{III}-catalyzed dehydrogenative cross-coupling reaction of a large range of simple benzene derivatives bearing arenes with directing groups is described. The key feature of this catalyst system is the application of $Cu(OAc)_2$ together with C_6Br_6 as a complex catalyst modifier. Notably, the discovery of this latter, less common additive opens the door to expand this CDC transformation to regio- and chemoselective arene–heteroarene cross-coupling reactions. Moreover, the application of the heteroaromatic reagents enables the amount of the coupling partner to be decreased down to three equivalents, thus rendering this transformation synthetically useful.

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[1] For recent reviews on direct arylation, see a) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147 – 1169; b) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem.* **2009**, *121*, 9976 – 10011; *Angew. Chem. Int. Ed.* **2009**, *48*, 9792 – 9826; c) B.-J. Li, S.-D. Yang, Z.-J. Shi, *Synlett* **2008**, 949 – 957; d) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174 – 238.

[2] For recent reviews on aryl–aryl bond formation, see a) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215 – 1292; b) G. P. McGlacken, L. M. Bateman, *Chem. Soc. Rev.* **2009**, *38*, 2447 – 2464; c) S.-L. You, J.-B. Xia, *Top. Curr. Chem.* **2010**, *292*, 165 – 194; d) J. A. Ashenhurst, *Chem. Soc. Rev.* **2010**, *39*, 540 – 548; for a recent reviews on CDCs of heteroaromatic compounds, see e) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068 – 5083; f) X. Bugaut, F. Glorius, *Angew. Chem.* **2011**, *123*, 7618 – 7620; *Angew. Chem. Int. Ed.* **2011**, *50*, 7479 – 7481; for a recent review on nonchelate-assisted C–H activations of simple arenes, see g) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem.* **2012**, *124*, 10382 – 10401; *Angew. Chem. Int. Ed.* **2012**, *51*, 10236 – 10254.

[3] For recent examples of Pd-catalyzed CDCs of two different arenes, see a) R. Li, L. Jiang, W. Lu, *Organometallics* **2006**, *25*, 5973 – 5975; b) J.-B. Xia, S.-L. You, *Organometallics* **2007**, *26*, 4869 – 4871; c) K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2007**, *129*, 11904 – 11905; d) T. W. Lyons, K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 4455 – 4464; e) B.-J. Li, S.-L. Tian, Z. Fang, Z.-J. Shi, *Angew. Chem.* **2008**, *120*, 1131 – 1134; *Angew. Chem. Int. Ed.* **2008**, *47*, 1115 – 1118; f) H. Li, J. Liu, C.-L. Sun, B.-J. Li, Z.-J. Shi, *Org. Lett.* **2011**, *13*, 276 – 279; g) G. Brasche, J. García-Fortanet, S. L. Buchwald, *Org. Lett.* **2008**, *10*, 2207 – 2210; h) Y. Wei, W. Su, *J. Am. Chem. Soc.* **2010**, *132*, 16377 – 16379; i) X. Zhao, C. S. Yeung, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 5837 – 5844; j) C. S. Yeung, X. Zhao, N. Borduas, V. M. Dong, *Chem. Sci.* **2010**, *1*, 331 – 336; k) X. Wang, D. Leow, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 13864 – 13867; l) L. Zhou, W. Lu, *Organometallics* **2012**, *31*, 2124 – 2127.

[4] For seminal reports on Pd-catalyzed CDCs involving heteroaromatic compounds, see a) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172 – 1175; b) D. R. Stuart, E. Villemure, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 12072 – 12073; for recent examples of dehydrogenative cross-coupling of arenes with heteroarenes, see c) Z. Li, L. Ma, J. Xu, L. Kong, X. Wu, H. Yao, *Chem. Commun.* **2012**, *48*, 3763 – 3765; d) T. A. Dwight, N. R. Rue, D. Charyk, R. Josselyn, B. DeBoef, *Org. Lett.* **2007**, *9*, 3137 – 3139; e) S. Potavathri, A. S. Dumas, T. A. Dwight, G. R. Naumiec, J. M. Hammann, B. DeBoef, *Tetrahedron Lett.* **2008**, *49*, 4050 – 4053; f) S. Potavathri, K. C. Pereira, S. I. Gorelsky, A. Pike, A. P. LeBris, B. DeBoef, *J. Am. Chem. Soc.* **2010**, *132*, 14676 – 14681; g) S. H. Cho, S. J. Hwang, S. Chang, *J. Am. Chem. Soc.* **2008**, *130*, 9254 – 9256; h) C.-Y. He, S. Fan, X. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12850 – 12852; i) M. Kitahara, N. Umeda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2011**, *133*, 2160 – 2162.

[5] J. Wencel-Delord, C. Nimphius, F. W. Patureau, F. Glorius, *Angew. Chem.* **2012**, *124*, 2290 – 2294; *Angew. Chem. Int. Ed.* **2012**, *51*, 2247 – 2251; for a related alkene – arene CDC reaction, see J. Wencel-Delord, C. Nimphius, F. W. Patureau, F. Glorius, *Chem. Asian J.* **2012**, *7*, 1208 – 1212.

[6] Rh^{III}-catalyzed intramolecular aryl – aryl coupling involving twofold C–H activation: K. Morimoto, M. Itoh, K. Hirano, T. Satoh, Y. Shibata, K. Tanaka, M. Miura, *Angew. Chem.* **2012**, *124*, 5455 – 5458; *Angew. Chem. Int. Ed.* **2012**, *51*, 5359 – 5362.

[7] For selected reviews on Rh-catalyzed C–H activation, see a) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31 – 41; b) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651 – 3678; c) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814 – 825; d) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212 – 11222; e) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624 – 655; f) J. Bouffard, K. Itami, *Top. Curr. Chem.* **2010**, *292*, 231 – 280.

[8] For selected, most recent publications on Rh^{III}-catalyzed C–H activation, see a) C. Grohmann, H. Wang, F. Glorius, *Org. Lett.* **2012**, *14*, 656 – 659; b) K.-H. Ng, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2012**, *14*, 272 – 275; c) H. Wang, F. Glorius, *Angew. Chem.* **2012**, *124*, 7430 – 7434; *Angew. Chem. Int. Ed.* **2012**, *51*, 7318 – 7322; d) N. Schröder, J. Wencel-Delord, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 8298 – 8301; e) Z. Shi, N. Schröder, F. Glorius, *Angew. Chem.* **2012**, *124*, 8216 – 8220; *Angew. Chem. Int. Ed.* **2012**, *51*, 8092 – 8096; f) C. Wang, H. Chen, Z. Wang, J. Chen, Y. Huang, *Angew. Chem.* **2012**, *124*, 7354 – 7357; *Angew. Chem. Int. Ed.* **2012**, *51*, 7242 – 7245; g) B.-J. Li, H.-Y. Wang, Q.-L. Zhu, Z.-J. Shi, *Angew. Chem.* **2012**, *124*, 4014 – 4018; *Angew. Chem. Int. Ed.* **2012**, *51*, 3948 – 3952; h) M. E. Tauchert, C. D. Incarvito, A. L. Rheingold, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2012**, *134*, 1482 – 1485; i) L. Zheng, J. Wang, *Chem. Eur. J.* **2012**, *18*, 9699 – 9704; j) Y. Du, T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 12074 – 12076; see also Ref. [6].

[9] For an early report, see F. W. Patureau, C. Nimphius, F. Glorius, *Org. Lett.* **2011**, *13*, 6346 – 6349.

[10] A. G. M. Barrett, T. Itoh, E. M. Wallace, *Tetrahedron Lett.* **1993**, *34*, 2233 – 2234.

[11] For details see the Supporting Information.

[12] For comparison, the prices of several commonly used oxidants for C–H bond activation are: inorganic reagents: $Na_2S_2O_8$ 5.2 €/mol; $Cu(OAc)_2{\cdot}H_2O$ 12.2 €/mol; Ag_2CO_3 573 €/mol; organic reagents: C_6Br_6 84.6 €/mol; *t*BuOOH 212 €/mol (0.5–0.6 M solution in decane); $PhI(OAc)_2$ 385 €/mol; $C_6H_2Br_4$ 529.5 €/mol; NFSI 955.3 €/mol.

[13] No reaction was observed when a 1,4-disubstituted benzene derivative (*p*-xylene) was used, probably because of the steric hindrance.

[14] The application of the benzamide bearing an iodo substituent in the *para* position led to the formation of a mixture of the desired product and a bromo-substituted biaryl product, the formation of which probably occurs through a Finkelstein type reaction.

[15] For a recent report concerning Rh^{III}-catalyzed C–H activation of indoles, see a) D. J. Schipper, M. Hutchinson, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 6910 – 6911; b) B. Zhou, Y. Yang, Y. Li, *Chem. Commun.* **2012**, *48*, 5163 – 5165; for a recent report concerning Rh^{III}-catalyzed cross-coupling of heterocycles, see N. Kuhl, M. N. Hopkinson, F. Glorius, *Angew. Chem.* **2012**, *124*, 8354 – 8358; *Angew. Chem. Int. Ed.* **2012**, *51*, 8230 – 8234.

[16] The deuteration experiments and their interpretation were inspired by the recent work of Hartwig and Simmons: E. M. Simmons, J. F. Hartwig, *Angew. Chem.* **2012**, *124*, 3120 – 3126; *Angew. Chem. Int. Ed.* **2012**, *51*, 3066 – 3072.

[17] For details of this study see the Supporting Information.

[18] K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2009**, *131*, 9651 – 9653.

[19] For a selected review on halogen bonding, see P. Metrangolo, H. Neukirch, T. Pilati, G. Resnati, *Acc. Chem. Res.* **2005**, *38*, 386 – 395.

